

SYNTHESIS OF 4A-ARYL-DECAHYDROISOQUINOLINES; FROM
1-METHYL-2-OXO-3-METHYLENE-4-(3'-METHOXYPHENYL)-4-(CARBOXYMETHYLENE) PIP
ERIDINE BY CYCLIZATION

Document Type: UTILITY

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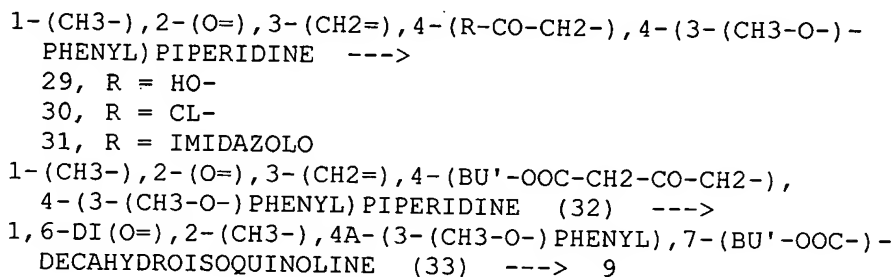
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Abstract:

This invention relates to a process for the production of 4aaryldecahydroisoquinolines where the aryl group is selected as 3methoxyphenyl. These compounds are morphine analogs and show utility similar to the known morphine, codeine, and thebaine. In this process particular novelty is asserted for the production of a nipecotic ester ethyl 4-(3'-methoxyphenyl)-1-methyl piperidine-3-carboxylate. Furthermore, novelty is asserted for the step of conversion of the nipecotates through cyclization to cis- or trans-tert-butyl 1,6-dioxo-4a-(3'-methoxyphenyl)-2-methyldecahydroisoquinoline-7-carboxylate, which may also be easily converted to the keto amide, trans-1,6-dioxo-4a-(3'-methoxyphenyl)-2-methyldecahydroisoquinoline.

Exemplary Claim:

1. IN A PROCESS OF PREPARING 4A-ARYLDECAHYDROISOQUINOLINES THE STEPS CONSISTING ESSENTIALLY OF THE CONVERSION OF NIPECOTATES TO SUBSTITUTED METHYLENEPIPERIDONE AND CARBOXYLIC RING FORMATION ACCORDING TO THE FOLLOWIN REACTION SYSTEM:



WHEREIN

4-CARBOXYMETHYL-4-(3'-METHOXYPHENYL)-1-METHYL-3METHYLENE-2-PIPERIDONE (29) IS CONVERTED TO AN IMIDAZOLIDE (31) BY THE ACTION OF CARBONYLDIIMIDAZOLE IN CHCL₃/THF AND SUBSEQUENTLY WITH THE MAGNESIUM ENOLATE OF TERT-BUTYL HYDROGEN MALONATE TO PRODUCE TERT-BUTYL 4-(4'-(4'-(3'-METHOXYPHENYL)-1'-METHYL-3'-METHYLENE-2'-OXOPIPERIDYL))-3-OXOBUTYRATE (32) AND THIS MATERIAL 32 IS CYCLIZED BY AN ALKALI METAL METHANOLATE DISSOLVE IN METHANOL TO TERT-BUTYL 1,6-DIOXO-4A(3'-METHOXYPHENYL)-2-METHYL-DECAHYDROISOQUINOLINE-7-CARBOXYLATE (33) AND SUBSEQUENTLY 33 IS TREATED WITH TRIFLUOROACETIC ACID IN BENZENE AND SUBSEQUENT RECOVERY BY RECRYSTALLIZATION FROM A BENZENE-HEXANE MIXTURE TO PRODUCE TRANS 1,6-DIOXO-4A-(3'-METHOXYPHENYL)-2-METHYL-DECAHYDROISOQUINOLINE (9).